

| CML Response Definitions | | |
|-----------------------------|---|--|
| Response | ELN | NCCN |
| <i>Hematologic Response</i> | | |
| CHR | Leukocyte count <10 x 10 ⁹ /L | Complete normalization of peripheral blood counts with leukocyte count <10 x 10 ⁹ /L |
| | Platelet count <450 x 10 ⁹ /L | Platelet count <450 x 10 ⁹ /L |
| | No immature cells, (ie, myelocytes, promyelocytes, or blasts) in peripheral blood | No immature cells, (ie, myelocytes, promyelocytes, or blasts) in peripheral blood |
| | Basophils <5% | |
| | Nonpalpable spleen | No signs and symptoms of disease with disappearance of palpable splenomegaly |
| <i>Cytogenetic Response</i> | | |
| CCyR | No Ph+ metaphases ^a | No Ph+ metaphases |
| PCyR | 1% - 35% Ph+ metaphases ^a | 1% - 35% Ph+ metaphases |
| Major | NA | 0% - 35% Ph+ metaphases (complete + partial) |
| Minor | 36% - 65% Ph+ metaphases ^a | >35% Ph+ metaphases |
| Minimal | 66% - 95% Ph+ metaphases ^a | NA |
| None | >95% Ph+ metaphases ^a | NA |
| <i>Molecular Response</i> | | |
| EMR | | <i>BCR-ABL1</i> transcripts ≤10% by QPCR (IS) at 3 and 6 months |
| MMR | Ratio <i>BCR-ABL1</i> to <i>ABL1</i> ≤0.1% on the International Scale | <i>BCR-ABL1</i> transcripts 0.1% by QPCR (IS) or ≥3-log reduction of <i>BCR-ABL1</i> mRNA from standardized baseline [†] |
| CMR or MUL [‡] | Undetectable <i>BCR-ABL1</i> by QPCR in 2 consecutive samples | No detectable <i>BCR-ABL1</i> mRNA by QPCR (IS)* |
| <i>Relapse</i> | | |
| | Loss of response (defined as hematologic or cytogenetic relapse or confirmed loss of MMR) | Any sign of loss of response (defined as hematologic or cytogenetic relapse) |
| | | 1-log increase in <i>BCR-ABL1</i> levels with loss of MMR should prompt bone marrow evaluation for loss of CCyR but is not itself defined as relapse |

*Using an assay with sensitivity of at least 4.5 logs below the standardized baseline. CMR is variably described, and is best defined by the assay's level of sensitivity (eg, MR 4.5).

[†]If qRT-PCR (IS) is not available.

[‡]ELN states the term *complete molecular response* (CMR) should be avoided and substituted with the term *molecularly undetectable leukemia* (MUL), with specification of the number of the control gene transcript copies [Baccarani M, et al. *Blood*. 2013;122(6):872-884.]

Abbreviations: CCyR=complete cytogenetic response; CHR=complete hematologic response; CML=chronic myeloid leukemia; CMR=complete molecular response; ELN=European LeukemiaNet; EMR=extramedullary relapse; MMR=major molecular response; MUL=molecularly undetectable leukemia; NA=not applicable; NCCN=National Comprehensive Cancer Network; PCyR=partial cytogenetic response; Ph+=Philadelphia chromosome-positive; QPCR or qRT-PCR=quantitative real time polymerase chain reaction.

^aOnly chromosome banding analysis (CBA) of marrow cell metaphases can be used to assess the degree of CyR, with at least 20 metaphases analyzed, and that fluorescence in situ hybridization (FISH) of blood interphase cell nuclei could substitute for CBA of marrow cell metaphases only for the assessment of CCyR, which is then defined by <1% *BCR-ABL1*-positive nuclei of at least 200 nuclei. [Baccarani M, et al. *Blood*. 2013;122(6):872-884.]

References: Baccarani M, et al. European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. *Blood*. 2013;122(6):872-884; Baccarani M, et al. European LeukemiaNet. Chronic myeloid leukemia: an update of concepts and management recommendations of European LeukemiaNet. *J Clin Oncol*. 2009;27(35):6041-6051; Baccarani M, et al. European LeukemiaNet. Evolving concepts in the management of chronic myeloid leukemia: recommendations from an expert panel on behalf of the European LeukemiaNet. *Blood*. 2006;108(6):1809-1820; Radich JP, et al. *NCCN Clinical Practice Guidelines in Oncology: Chronic Myelogenous Leukemia*. Version 1.2016 (09/09/2015). Accessed March 8, 2016 at http://www.nccn.org/professionals/physician_gls/pdf/cml.pdf.



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